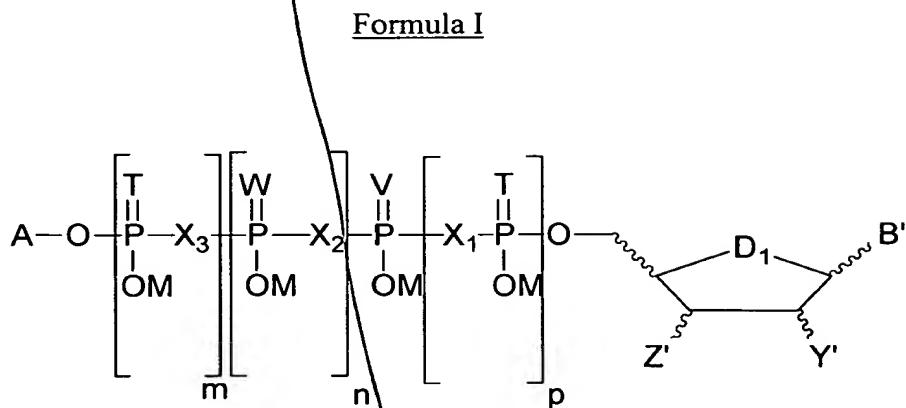


WHAT IS CLAIMED:

1. The compound comprising general formula I, or salts thereof:



wherein:

X₁, X₂, and X₃ are selected from the group consisting of independently or together oxygen, 10 methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, W, and V are independently or together oxygen or sulfur;

m= 0,1 or 2;

n= 0,1, or 2;

15 p= 0,1, or 2 ;

M= H or a pharmaceutically-acceptable inorganic or organic counterion;

D₁ =O or C;

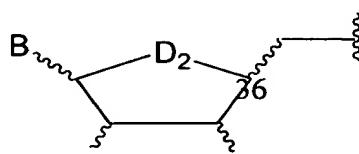
B' is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the 5' position of the furanose or carbocycle via the 9- or 1- position, respectively;

20 Y' =H or OR₁;

Z' =H or OR₂;

A is elected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms; or

A is a nucleoside residue which is defined as:



and which is linked to the phosphate chain via the 5' position of the furanose or carbocycle; wherein:

5 $Z = H$ or OR_3 ;

Y = H or OR_4 ;

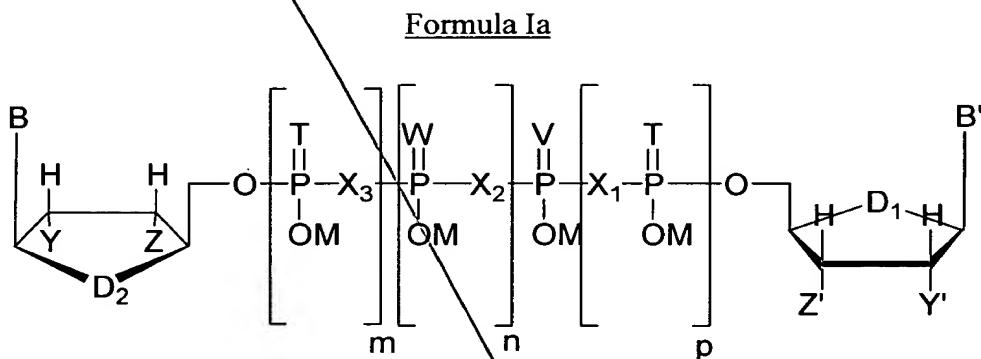
$D_2 = O$ or C;

B is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the sugar or carbocycle via the 9- or 1- position, respectively;

10 R_1, R_2, R_3 , and R_4 are H, provided that at least one of the four is a residue according to general formulas II and III which is linked to the 2' or 3' furanose or carbocycle hydroxyl oxygen via a carbon atom;

wherein further provisions are that when D_1 and D_2 are oxygen, the furanose is preferably in the β -configuration; most preferably in the β -D-configuration;

15 wherein preferred compounds of general Formula I are molecules whose structures fall within the definitions of Formula Ia and Formula Ib:



wherein:

20 X_1, X_2 , and $X_3 = O$;

T, V, and W = O;

M = H, NH_4^+ , Na^+ or other pharmaceutically-acceptable inorganic or organic counterion;

Y' = H, OH, or OR_1 , where R_1 falls under the definition of general formula II;

Z' = OH or OR_2 , where R_2 falls under the definition of general formula II;

25 Z = OH or OR_3 , where R_3 falls under the definition of general formula II;

Y = H, OH, or OR_4 , where R_4 falls under the definition of general formula II;

~~D₁ =O;~~

~~D₂ =O or C;~~

~~B and B' are purine or pyrimidine residues according to general formulas IV and V;~~

~~m and p= 0,1 or 2;~~

5 n= 0 or 1;

such that the sum of m+n+p is from 1 to 5; or

~~X₁, X₂, and X₃=O;~~

~~T, V, and W= O;~~

~~M= H, NH4⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion ;~~

10 Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula III;

~~Z'= OH or OR₂, where R₂ falls under the definition of general formula III;~~

~~Z= OH or OR₃, where R₃ falls under the definition of general formula III;~~

~~Y= H, OH, or OR₄, where R₄ falls under the definition of general formula III;~~

~~D₁ =O;~~

15 D₂ =O or C;

~~B and B' are purine or pyrimidine residues according to general formulas IV and V;~~

~~m and p= 0,1 or 2;~~

~~n= 0 or 1;~~

such that the sum of m+n+p is from 1 to 5; or

20 X₁ and X₃=O;

X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

~~T, V, and W= O;~~

~~M= H, NH4⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion ;~~

25 Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula II;

~~Z'= OH or OR₂, where R₂ falls under the definition of general formula II;~~

~~Z= OH or OR₃, where R₃ falls under the definition of general formula II;~~

~~Y= H, OH, or OR₄, where R₄ falls under the definition of general formula II;~~

~~D₁ =O;~~

30 D₂ =O or C;

~~B and B' are purine or pyrimidine residues according to general formulas IV and V;~~

~~m and p= 0,1 or 2;~~

~~n= 1;~~

~~such that the sum of m+n+p is from 1 to 5; or~~

~~X₁ and X₃=O;~~

~~X₂ is selected from the group consisting of methylene, monochloromethylene,~~

~~5 dichloromethylene, monofluoromethylene, difluoromethylene, and imido;~~

~~T, V, and W= O;~~

~~M= H, NH4⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;~~

~~Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula III;~~

~~Z'= OH or OR₂, where R₂ falls under the definition of general formula III;~~

~~10 Z= OH or OR₃, where R₃ falls under the definition of general formula III;~~

~~Y= H, OH, or OR₄, where R₄ falls under the definition of general formula III;~~

~~D₁=O;~~

~~D₂ is O or C;~~

~~B and B' are purine or pyrimidine residues according to general formulas IV and V;~~

~~15 m and p= 0,1 or 2;~~

~~n=1;~~

~~such that the sum of m+n+p is from 1 to 5; or~~

~~X₁ and X₃=O;~~

~~X₂ is selected from the group consisting of methylene, monochloromethylene,~~

~~20 dichloromethylene, monofluoromethylene, difluoromethylene, and imido;~~

~~T= S;~~

~~V and W=O;~~

~~M= H, NH4⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;~~

~~Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula II;~~

~~25 Z'= OH or OR₂, where R₂ falls under the definition of general formula II;~~

~~Z= OH or OR₃, where R₃ falls under the definition of general formula II;~~

~~Y= H, OH, or OR₄, where R₄ falls under the definition of general formula II;~~

~~D₁=O;~~

~~D₂=O or C;~~

~~30 B and B' are purine or pyrimidine residues according to general formulas IV and V;~~

~~m, n, and p= 1; or~~

~~X₁ and X₃=O;~~

~~X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;~~

~~T= S;~~

~~V and W=O;~~

5 M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula III;

Z'= OH or OR₂, where R₂ falls under the definition of general formula III;

Z= OH or OR₃, where R₃ falls under the definition of general formula III;

10 Y= H, OH, or OR₄, where R₄ falls under the definition of general formula III;

D₁ =O;

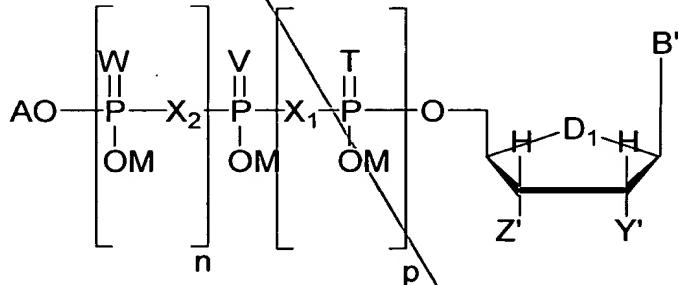
D₂ =O or C;

B and B' are purine or pyrimidine residues according to general formulas IV and V;

m, n, and p= 1; or

15

Formula Ib



where for general formula I, m=0, and all other definitions remain the same;

20 wherein:

A is elected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;

X₁ and X₂= O;

T, V, and W= O;

25 M= H, NH₄, Na or other pharmaceutically-acceptable inorganic or organic counterion;

~~Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula II;~~

~~Z'= H, OH or OR₂, where R₂ falls under the definition of general formula II;~~

~~With the provision that at least one of Y' and Z' is OR₁ or OR₂;~~

~~D₁ =O or C;~~

5 B' is purine or pyrimidine residue according to general formulas IV and V;

n and p are 0,1, or 2 such that the sum of n+p is from 1 to 3; or

A is selected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;

X₁ and X₂= O;

10 T, V, and W= O;

M is selected from the group consisting of H, NH4, Na and other pharmaceutically-acceptable inorganic or organic counterion;

~~Y'= OR₁, where R₁ falls under the definition of general formula III;~~

~~Z'= OR₂, where R₂ falls under the definition of general formula III;~~

15 D₁ =O or C;

B' is purine or pyrimidine residue according to general formulas IV and V;

n and p are 0,1, or 2 such that the sum of n+p is from 1 to 3; or

A is selected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;

20 X₁ and X₂= O;

T and V= O;

W=S;

M= H, NH4, Na or other pharmaceutically-acceptable inorganic or organic counterion;

~~Y'= H, OH, or OR₁, where R₁ falls under the definition of general formula II;~~

25 Z'= H, OH or OR₂, where R₂ falls under the definition of general formula II;

~~With the provision that at least one of Y' and Z' is OR₁ or OR₂;~~

D₁ =O or C;

B' is purine or pyrimidine residue according to general formulas IV and V;

p is 0,1, or 2 such that the sum of n+p is from 1 to 3;

30 n=1; or

A is selected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;

30

~~X₁ and X₂ = O;~~

~~T and V = O;~~

~~W = S;~~

~~M is selected from the group consisting of H, NH₄, Na and other pharmaceutically-acceptable~~

~~5 inorganic or organic counterion;~~

~~Y' = OR₁, where R₁ falls under the definition of general formula III;~~

~~Z' = OR₂, where R₂ falls under the definition of general formula III;~~

~~D₁ = O or C;~~

~~B' is purine or pyrimidine residue according to general formulas IV and V;~~

~~10 p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;~~

~~n=1; or~~

~~A is selected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;~~

~~X₁ = O;~~

~~15 X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;~~

~~T, V, and W = O;~~

~~M is selected from the group consisting of H, NH₄, Na and other pharmaceutically-acceptable inorganic or organic counterion;~~

~~20 Y' = H, OH, or OR₁, where R₁ falls under the definition of general formula II;~~

~~Z' = H, OH or OR₂, where R₂ falls under the definition of general formula II;~~

~~With the provision that at least one of Y' and Z' is OR₁ or OR₂;~~

~~D₁ = O or C;~~

~~B' is purine or pyrimidine residue according to general formulas IV and V;~~

~~25 p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;~~

~~n=1; or~~

~~A is selected from the group consisting of M, alkyl, cycloalkyl, aralkyl, aryl, and acylthioalkyl, with or without substituents or heteroatoms;~~

~~X₁ = O;~~

~~30 X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;~~

~~T, V, and W = O;~~

~~M is selected from the group consisting of H, NH₄, Na and other pharmaceutically-acceptable inorganic or organic counterion;~~

$Y' = H, OH, \text{ or } OR_1$, where R_1 falls under the definition of general formula III;

$Z' = H, OH$ or OR_2 , where R_2 falls under the definition of general formula III;

5 $D_1 = O$ or C ;

B' is purine or pyrimidine residue according to general formulas IV and V;

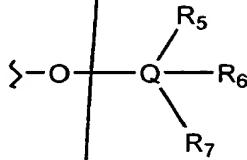
p is 0, 1, or 2 such that the sum of $n+p$ is from 1 to 3;

n=1;

wherein, for compounds according to Formula Ia or Ib, where $Y' = OR_1$, $Z' = OR_2$, $Z = OR_3$

10 and/or $Y = OR_4$, at least one of the four must be a residue which is linked directly to the corresponding 2' or 3' hydroxyl oxygen of the furanose or carbocycle via a carbon atom; and for the most part, this residue falls within the scope of formula II or formula III:

Formula II



5 wherein:

O is the corresponding 2' or 3' oxygen of the furanose or carbocycle;

R₅, R₆, and R₇ are selected from the group consisting of H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety defined according to formula II is an ether; or

10 provided that R₅ and R₆ are taken together to mean oxygen or sulfur doubly bonded to Q, and R₇ is selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety defined according to formula II is an ester or thioester; or

provided that R₅ and R₆ are taken together to mean oxygen or sulfur doubly bonded to Q, and

15 R₇ is amino or mono- or disubstituted amino, where the substituents are selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety according to formula III is a carbamate or thiocarbamate; or

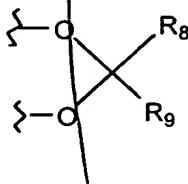
provided that R₅ and R₆ are taken together to mean oxygen or sulfur doubly bonded to Q, and R₇ is selected from the group consisting of alkoxy, cycloalkoxy, aralkyloxy, aryloxy,

20 substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula II is a carbonate or thiocarbonate; or

provided that R₅ and R₆ are taken together to mean oxygen or sulfur doubly bonded to Q and both the 2' and 3' oxygens of the furanose are directly bound to Q to form a cyclical carbonate or thiocarbonate, R₇ is not present; or

25

Formula III



wherein:

O is the 2' and 3' oxygens of the furanose or carbocycle; and
the 2' and 3' oxygens of the furanose or carbocycle are linked by a common carbon atom to

5 form a cyclical acetal, cyclical ketal, or cyclical orthoester; and
for cyclical acetals and ketals, R₈ and R₉ are selected from the group consisting of
independently hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted
aryl; or may be joined together to form a homocyclic or heterocyclic ring composed of 3 to 8
atoms, or

10 for cyclical orthoesters, R₈ is selected from the group consisting of hydrogen, alkyl,
cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl,
and R₉ is selected from the group consisting of alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy,
substituted aralkyloxy, and substituted aryloxy;

15 wherein, in general, R₅ to R₉ are selected from the group consisting of, but are not limited to,
the following:

a) alkyl groups are from 1 to 8 carbons, either straight chained or branched, with or without
unsaturation and with or without heteroatoms;

b) cycloalkyl groups are from 3 to 8 carbons, with or without unsaturation, and with or
without heteroatoms;

20 c) aralkyl groups are from 1 to 5 carbons in the alkyl portion, and are monocyclic or
polycyclic moieties from 4 to 8 carbons per ring, with or without heteroatoms, in the aryl
portion;

d) aryl groups are monocyclic or polycyclic moieties from 4 to 8 carbons, with or without
heteroatoms; and

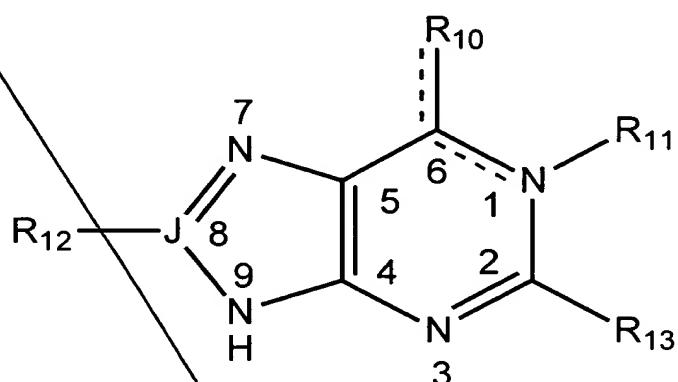
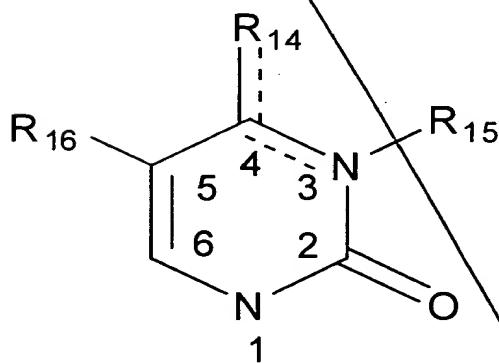
25 these groups may or may not bear substituents; or

wherein preferred substituents on the foregoing groups are selected from the group consisting
of, but are not limited to, hydroxy, nitro, methoxy, fluoro, chloro, bromo, iodo, methyl, ethyl,
propyl, butyl, thioalkyl, alkoxy, carboxyl, cyano, amino, substituted amino, trifluoromethyl,
phenyl, cyclopropyl, cyclopentyl, and cyclohexyl; and

30 wherein preferred heteroatoms are selected from the group consisting of oxygen, nitrogen,
and sulfur;

~~B and B' are independently a purine residue, as in formula IV, linked through the 9- position, or a pyrimidine residue, as in formula V, linked through the 1- position; wherein, when D₁ and D₂ are oxygen, the ribosyl moieties are in the preferred D- configuration, but may be L-, or D- and L-;~~

5

Formula IVFormula V

Ar
wherein:

R₁₀ and R₁₄ are selected from the group consisting of hydroxy, oxo, amino, mercapto, alkylthio, alkyloxy, aryloxy, alkylamino, cycloalkylamino, aralkylamino, arylamino,

15

diaralkylamino, diarylamino, or dialkylamino, where the alkyl groups are optionally linked to form a heterocycle; or

R₁₀ and R₁₄ are acylamino, provided that they incorporate an amino residue from the C-6 position of the purine or the C-4 position of the pyrimidine; or

5 when R₁₀ in a purine or R₁₄ in a pyrimidine has as its first atom nitrogen, R₁₀ and R₁₁ or R₁₄ and R₁₅ are taken together to form a 5-membered fused imidazole ring, optionally substituted on the etheno ring with R₅-R₉ selected from the group consisting of alkyl, cycloalkyl, aralkyl, or aryl moieties, as described above;

J is carbon or nitrogen, with the provision that when nitrogen, R₁₂ is not present;

10 R₁₁ is hydrogen, O or is absent;

R₁₂ is selected from the group consisting of hydrogen, alkyl, azido, alkylamino, arylamino, aralkylamino, alkoxy, aryloxy, aralkyloxy, alkylthio, arythio, aralkylthio, and ω -A(C₁-₆alkyl)B- wherein A and B are selected from the group consisting of independently amino, mercapto, hydroxy and carboxyl;

15 R₁₃ is selected from the group consisting of hydrogen, chlorine, amino, monosubstituted amino, disubstituted amino, alkylthio, arylthio, and aralkylthio, where the substituent on sulfur contains up to a maximum of 20 carbon atoms, with or without unsaturation;

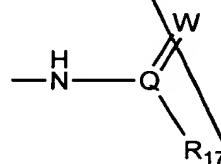
R₁₅ is selected from the group consisting of hydrogen, and acyl, such as acetyl, benzoyl, phenylacetyl, with or without substituents;

20 R₁₆ is selected from the group consisting of hydrogen, methyl, alkyl, halo, alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl;

wherein compounds where R₁₀ or R₁₄ is acylamino fall within the scope of formula VI:

Formula VI

25



wherein:

1. NH is the amino residue at the C-6 position in a purine or the amino residue at the C-4 position in a pyrimidine;

2. Q is a carbon atom;

3. W is oxygen or sulfur;

4. R₁₇ is amino or mono- or disubstituted amino such that the moiety according to formula VI is a urea or thiourea; or

5. R₁₇ is selected from the group consisting of alkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula VI is a carbamate or thiocarbamate; or

6. R₁₇ is selected from the group consisting of alkyl, cycloalkyl, aralkyl, and aryl, with or without substituents or heteroatoms, such that the moiety according to formula VI is an amide.

2. The compound according to Claim 1, wherein said compound is fluorescently labeled and used as a biochemical probe for the P₂T receptor.

3. A method of preventing or treating diseases or conditions associated with platelet aggregation comprising:

4. administering to a subject a pharmaceutical composition comprising a therapeutic effective amount of P₂T receptor antagonist compound, wherein said amount is effective to bind the P₂T receptors on platelets and inhibit ADP-induced platelet aggregation.

5. The method of Claim 3, wherein said P₂T receptor antagonist compound comprises said general formula I, or salts thereof.

25

6. The method according to Claim 3, wherein said administering of said antagonist compound is used to reduce the incidence of dose-related adverse side effects of other therapeutic agents used to prevent, manage or treat platelet aggregation disorders.

6. The method according to Claim 3, wherein said administering is systemic administration of said compound.

7. The method according to Claim 6, wherein said systemic administration is administration of an injectable form of said compound, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.

8. The method according to Claim 6, wherein said systemic administration of said compound is accomplished by administering an oral form of said compound, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.

9. The method according to Claim 6, wherein said systemic administration is administration of said compound in a form of a transdermal patch or a transdermal pad, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.

10. The method according to Claim 6, wherein said systemic administration is administration of a liquid/liquid suspension of said compound via nose drops or nasal spray, or administration of a nebulized liquid to oral or nasopharyngeal airways of said subject, such that a therapeutically effective amount of said compound inhibits platelet aggregation.

11. The method according to Claim 6, wherein said systemic administration comprises infusion of said compound to target platelets via a device selected from a group consisting of a pump catheter system and a continuous or selective release device.

12. The method according to Claim 6, wherein said systemic administration is administration of a suppository form of said compound, such that a therapeutically effective

amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.

13. The method according to Claim 6, wherein said systemic administration is vaginal
5 administration in dosage unit formulations containing conventional non-toxic
pharmaceutically acceptable carriers, adjuvants and vehicles.

14. The method according to Claim 6, wherein said compound is administered to a patient
by an intravitreal delivery.

10
15. The method according to Claim 6, wherein said systemic administration is
administration of an intra-operative instillation of a gel, cream, powder, foam, crystals,
liposomes, spray or liquid suspension form of said compound, such that a therapeutically
effective amount of said compound contracts the target platelets of said patient via systemic
15 absorption and circulation.

20
25
16. ~~The method according to Claim 3, wherein said diseases or conditions associated with~~
~~platelet aggregation are disorders or procedures characterized by thrombosis, primary arterial~~
~~thrombotic complications of atherosclerotic disease, thrombotic complications of~~
~~interventions of atherosclerotic disease, thrombotic complications of surgical or mechanical~~
~~damage, mechanically – induced platelet activation, shunt occlusion, thrombosis secondary to~~
~~vascular damage and inflammation, indications with a diffuse thrombotic/platelet~~
~~consumption component, venous thrombosis, coronary arterial thrombosis, pathological~~
~~effects of atherosclerosis and arteriosclerosis, platelet aggregation and clot formation in blood~~
~~and blood products during storage, chronic or acute states of hyper-aggregability, reocclusion~~
~~of an artery or vein following fibrinolytic therapy, platelet adhesion associated with~~
~~extracorporeal circulation , thrombotic complications associated with thrombolytic therapy,~~
~~thrombotic complications associated with coronary and other angioplasty, and thrombotic~~
~~complications associated with coronary artery bypass procedures.~~

17. The method according to Claim 16, wherein said disorders or procedures associated with thrombosis are unstable angina, coronary angioplasty, and myocardial infarction.

5 18. The method according to Claim 16, wherein said primary arterial thrombotic complications of atherosclerosis are thrombotic stroke, peripheral vascular disease, and myocardial infarction without thrombolysis.

10 19. The method according to Claim 16, wherein said thrombotic complications of interventions of atherosclerotic disease are angioplasty, endarterectomy, stent placement, coronary and other vascular graft surgery.

15 20. The method according to Claim 16, wherein said thrombotic complications of surgical or mechanical damage are tissue salvage following surgical or accidental trauma, reconstructive surgery including skin flaps, and "reductive" surgery such as breast reduction.

20 21. The method according to Claim 16, wherein said mechanically – induced platelet activation is caused by cardiopulmonary bypass resulting in microthromboembolism and storage of blood products.

22. The method according to Claim 16, wherein said shunt occlusion is renal dialysis and plasmapheresis.

25 23. The method according to Claim 16, wherein said thromboses secondary to vascular damage and inflammation are vasculitis, arteritis, glomerulonephritis and organ graft rejection.

24. The method according to Claim 16, wherein said indications with a diffuse thrombotic/platelet consumption component are disseminated intravascular coagulation,

thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, heparin-induced thrombocytopenia, and pre-eclampsia/eclampsia.

25. The method according to Claim 16, wherein said venous thrombosis are deep vein
5 thrombosis, veno-occlusive disease, hematological conditions, and migraine.

26. The method according to Claim 25, wherein said hematological conditions are
thrombocythemia and polycythemia.

10 27. The method according to Claim 16, wherein said coronary arterial thrombosis is
associated with unstable angina, coronary angioplasty and acute myocardial infarction.

28. The method according to Claim 16, wherein pathological effects of atherosclerosis
and arteriosclerosis are arteriosclerosis, acute myocardial infarction, chronic stable angina,
15 unstable angina, transient ischemic attacks, and strokes, peripheral vascular disease, arterial
thrombosis, preeclampsia, embolism, restenosis or abrupt closure following angioplasty,
carotid endarterectomy, and anastomosis of vascular grafts.

20 29. The method according to Claim 16, wherein said chronic or acute states of hyper-
aggregability is caused by DIC, septicemia, surgical or infectious shock, post-operative and
post-partum trauma, cardiopulmonary bypass surgery, incompatible blood transfusion,
abruptio placenta, thrombotic thrombocytopenic purpura, snake venom and immune diseases.

30. The method according to Claim 16, wherein said reocclusion of an artery or vein
25 following fibrinolytic therapy is inhibited by internal administration of said compound with a
fibrinolytic agent.

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cancel*

Claim 31
31. The method according to Claim 30, wherein said fibrinolytic agent is selected from a group consisting of natural or synthetic products which directly or indirectly cause lysis of a fibrin clot.

5 32. The method according to Claim 30, wherein said fibrinolytic agent is a plasminogen activator selected from a group consisting of anistreplase, urokinase (UK), pro-urokinase (PUK), streptokinase (SK), tissue plasminogen activator (tPA) and mutants, or variants thereof, which retain plasminogen activator activity.

10 33. The method according to Claim 32, wherein said variants are selected from a group consisting of variants which have been chemically modified, variants which one or more amino acids have been added, deleted or substituted or variants with one or more modified functional domains.

15 34. The method according to Claim 33, wherein said modified functional domains are added, deleted or altered by combining the active site of one plasminogen activator or fibrin binding domain of another plasminogen activator or fibrin binding molecule.